

Reserpine and Chlorpromazine

Their Use in Alcoholic and Geriatric Patients

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AT THIS TIME a report of the direct clinical results of reserpine and chlorpromazine in hospitalized geriatric and alcoholic patients does not appear to be as important as a discussion of some of the less obvious implications that have been noted in the use of these drugs in the treatment of such patients.

The observations here discussed deal primarily with the use of reserpine and chlorpromazine in 33 chronic geriatric patients, and the use of chlorpromazine in 15 newly admitted patients with alcoholism.

Reserpine

In 23 chronic geriatric patients who received reserpine, the effects seemed to vary according to the dosage. From 0.5 mg. to 6.0 mg. daily was used, according to the patient's ability to tolerate the medication and according to the apprehension of the individual physicians using the drug. Agitation and disturbed behavior was decreased. The patient became more tractable, more cooperative and less demanding. Confusion, disorientation, loss of memory and other signs of organic involvement did not appear to be greatly affected, nor did the course of depressions seem to be greatly altered. Some of the bedridden patients became ambulatory or at least were able to sit in a wheelchair for part of the day. Three were eventually able to be considered for a leave to stay with relatives. On the other hand, the lethargy that was produced in some patients was a deterrent to further use of the medication after a few weeks. These results would appear to corroborate the general information at present available about reserpine, with but one additional and perhaps important finding.

In a group of nine geriatric patients to whom reserpine was given, cholesterol and blood lipoprotein determinations were obtained.* These patients

• Although reserpine and chlorpromazine had tranquilizing effect on a number of geriatric and alcoholic patients in a state hospital, several complicating results were noted, some with a bearing on the patients' health and others that might affect the assignment of personnel.

Lipoprotein studies carried out on patients receiving reserpine seemed to indicate that a reduction in the blood levels of the denser lipoprotein molecules took place during therapy.

Several elderly patients receiving chlorpromazine died of diseases that were not as sharply manifest by symptoms as they might be expected to be. Hence the need for closer observation than a limited staff could afford seemed a matter for consideration. Another consideration of the same order was the possible need for increased personnel for psychotherapy in light of the more receptive condition of the patients.

were given dosages from 1.0 mg. to 2.0 mg. daily for a three-week period and were then given 6.0 mg. daily. In five of these patients this dosage was continued for a period of more than six weeks; in the other four the medication was reduced or discontinued within a one to six-week period because increased lethargy was considered detrimental to the patient. None of the nine patients showed any considerable psychiatric improvement. However, within this entire group seven patients showed a definite drop in the blood level of the heavier and more compact lipoprotein molecules (S_r 0-12). Three weeks after discontinuance of the drug, the content of these molecules in the blood had returned to the premedication level in only one of the seven patients. Six weeks after discontinuance, results were available on five patients. In only one of them was the amount of S_r 0-12 lipoprotein back to premedication level, although in the others it was showing a gradual return. Two of the nine patients showed no response. In the next lighter group of molecules (S_r 12-20) there was less change, although the same seven patients showed indications of a drop. Of these seven, five showed a return to premedication level within three weeks after termination of the

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*These determinations and the processing of data obtained, as well as the lipoprotein studies on the geriatric patients receiving chlorpromazine were carried out by John Gofman, M.D., and Beverly Strisower, A.B., Department of Medical Physics, University of California.

drug. Two again showed no response. In the seven patients who showed a lipoprotein drop, blood cholesterol determinations during the period of medication showed a corresponding reduction. Again the two patients showing no response in the blood lipoprotein levels showed no appreciable change in blood cholesterol. It appeared further that the patients with higher initial blood lipoproteins and blood cholesterol levels showed a greater drop on medication.

Because of the small series, these results cannot be considered conclusive, but they do give a strong indication that reserpine affects the body's lipoprotein metabolism in some way not yet clearly understood. It indicates that reserpine has its strongest effects on the denser lipoprotein molecules (S_r 0-12). Other studies¹ indicate that desiccated thyroid also influences the level of these molecules although not apparently in the same manner. Further studies to give more conclusive information on this phenomenon are in preparation.

Chlorpromazine

Results with the use of chlorpromazine on newly admitted alcoholic patients, many of whom either were having or seemed about to have delirium tremens or alcoholic hallucinosis, did not vary substantially from the general trends indicated in the pharmaceutical circulars. Restlessness, apprehension, tremors and nausea and vomiting were reduced and on occasion eliminated with a dosage of 200 mg. to 400 mg. daily for periods varying from three days to two weeks depending upon the severity of symptoms. The need for other sedation seemed to be reduced. The confusion, disorientation and memory loss did not appear to be dramatically affected by the use of the drug. The transitory depressions that occur on recovery from an acute bout of alcoholism still appeared. Generally it seemed that the patient became more tranquil and less demanding, and that he tended to complain less of physical symptoms. Administration of chlorpromazine with other specific medication for concurrent illness appeared to be a desirable method of managing the patient during the early days of hospitalization.

In an attempt to evaluate the effects of chlorpromazine on a smaller scale with chronic geriatric patients, a group of ten men was selected. Seven of them were over and three under age 60. The dosage was gradually increased from 50 mg. daily to 400 mg. daily. The only untoward side effect observed was subclinical jaundice which developed in one of the younger patients. However, five of the patients over 60 years of age died within six weeks of starting the drug. These results were not at all in keeping with the observations in other groups in the

same hospital either with reserpine or chlorpromazine. An investigation of the causes of death indicated the following: Three patients showed some clinical signs of bronchopneumonia. In one this disease was confirmed at autopsy. One patient died in a diabetic coma, and at autopsy pulmonary edema with questionable pneumonia was noted. In the fifth case indications of mesenteric thrombosis and pronounced aortic atheromatosis were observed at postmortem examination.

In all five deaths the terminal illnesses appeared to be rather acute. Several physicians observing the patients were all impressed with their noncritical appearance in the terminal state. None of the patients had any of the usual indications of drug intolerance other than that of fever. There were no indications whatsoever that chlorpromazine was directly a cause of death, but conclusions drawn at the hospital from analysis of each case were that chlorpromazine lessened the clinical manifestations of the concurrent illnesses by its tranquilizing effect. The apprehension, anxiety and restlessness of the patient in distress were masked and distorted to such a degree that the medical staff was lulled into a false sense of security until the patient entered an irreversible terminal state.

Blood lipoprotein determinations were carried out in this group as well. No significant lowering of the blood lipoprotein or cholesterol levels was apparent in the short time the drug was administered. Further studies are indicated, since of necessity these findings are inconclusive.

DISCUSSION

In limited experience with the use of these drugs in newly admitted alcoholic patients and on the chronic geriatric services, it was observed that the tranquilizing effects of these drugs, while desirable, can be hazardous as well. The administration of these drugs to a large number of patients requires critical observations that are not within the realistic capabilities of the personnel of the usual grossly understaffed state hospital ward. It appears, therefore, that the time and effort saved in coping with the agitated, disturbed and demanding patient must be given over to closer observation. Again, when the withdrawn patients improve, additional time must be spent with them in carrying out a positive treatment program in which the tranquilizing drugs are but a part. This holds true in the alcoholic group as well. Although less time was spent in dealing with the individual's apprehension, more time had to be spent in observing him for side effects and more time had to be spent on some occasions in encouraging the patient to participate in the active treatment program.

CONCLUSIONS

Experiences with reserpine and chlorpromazine led to the following impressions:

Tranquilizing drugs are valuable adjuncts to therapy, but the serious hazards associated with them must not be underestimated on overcrowded, understaffed wards.

As long as we have before us the goal of suppression of symptoms and not the treatment of the sociobiological entity of the patient, we can claim only partial results and we must be prepared to treat recurrences of illness.

Reserpine, but not chlorpromazine, appears to cause a lowering of the same lipoprotein molecules in the blood as desiccated thyroid, but not in the same manner.

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REFERENCE

1. Strisower, B., Gofman, J. W., et al.: Effect of long-term administration of desiccated thyroid on serum lipoprotein and cholesterol levels, *J. Clin. Endoc. & Metab.*, Vol. XV, No. 1, Jan. 1955.

Correction

In the article, "Surgical Treatment of Pulmonary Tuberculosis—A Decade of Change," by John S. Chambers, M.D., in the June 1956 issue of *CALIFORNIA MEDICINE*, an error was made in the printing of the summary. The phrase, "in favor of extraperiosteal plombage, particularly in older, poor risk patients," which appeared at the end of the third paragraph of the summary, should have been printed at the end of the fourth paragraph instead.

The third and fourth paragraphs should read:

Pneumoperitoneum has replaced other forms of temporary collapse. Pneumothorax, phrenic nerve interruption and pneumonolysis have been abandoned.

The use of permanent collapse measures as definitive treatment has decreased, thoracoplasty and extrapleural pneumothorax having been virtually abandoned in favor of extraperiosteal plombage, particularly in older, poor risk patients.